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| APPLICATION NO.  | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.      | CONFIRMATION NO. |
|--|-------------|----------------------|--------------------------|------------------|
| 10/591,465   | 06/29/2007  | Pascal Perriat       | 71247-0065               | 1859             |
| 22902  | 7590        | 04/24/2012           |                          |                  |
| CLARK & BRODY<br>1700 Diagonal Road, Suite 510<br>Alexandria, VA 22314 |             |                      | EXAMINER<br>DO, PENSEE T |                  |
|  |             |                      | ART UNIT                 | PAPER NUMBER     |
|  |             |                      | 1641                     |                  |
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|  |             |                      | 04/24/2012 PAPER         |                  |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

**Office Action Summary****Application No.**

10/591,465

**Applicant(s)**

PERRIAT ET AL.

**Examiner**

PENSEE DO

**Art Unit**

1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 29 April 2011.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on \_\_\_\_; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 5) ☒ Claim(s) 1-30 is/are pending in the application.
- 5a) Of the above claim(s) 25-30 is/are withdrawn from consideration.
- 6) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 7) ☒ Claim(s) 1-24 is/are rejected.
- 8) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 9) ☒ Claim(s) 1-30 are subject to restriction and/or election requirement.

**Application Papers**

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 12) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-853)  
Paper No(s)/Mail Date 6/22/11; 1/3/12
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 2, 2011 has been entered.

### ***Priority***

This application 10591465, **PG Pub. No.** 20070281324 filed 06/29/2007 is a national stage entry of PCT/FR05/00491 , International Filing Date: 03/02/2005 and claims foreign priority to a French application 0402115 , filed 03/02/2004.

### ***Information Disclosure Statement***

The IDS submitted on January 3, 2012; and June 22, 2011 have been acknowledged and considered.

### ***Claims Status***

Claims 1-30 are pending.

Claims 25-30 are withdrawn.

Claims 1-24 are being examined.

### ***Claim Objections***

Claim 16 is objected to because of the following informalities: claim 16 recites "Np" twice. Appropriate correction is required.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 7-15, 18-22, 24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14-16, 19-22, 24 and 31 of copending Application No. 12/293,486 (*copending appl. '486*) in view of Li et al (US 2004/0075083).

Copending appl. '486 claims nanoparticles comprising a core and shell structure, wherein the core is made up of rare earth metal oxide such as europium and a coating of thickness between 1-10 nm.

However, copending appl. '486 fails to teach a polysiloxane coating and at least one biological ligand grafted by covalent bonding to the polysiloxane coating.

Li teaches Europium (Eu)-containing fluorescent nanoparticles comprising an aluminum oxide framework having Europium activator, and at least one energy reservoir selected from Mg, Ca, Sr and Ba and one co-activator such as Sc, Y, La, Ce, Pr, Nd, etc...(see [0006]). The nanoparticles are coated with a silicon-containing compound such as siloxane or polysiloxane which contains functional groups through which biological molecules such as proteins, nucleic acids, carbohydrate are bound (see [0036], [0026]).

Therefore, it would have been obvious to one of ordinary skill in the art to coat the nanoparticle copending appl. '486 with a functionalized polysiloxane coating as taught by Li so that the nanoparticles of copending appl. '486 can be used as labels in

biological assays. One of ordinary skill in the art would have a reasonable expectation of success when combining the teachings of Li and copending appl. '486 because both teach using nanoparticles that are doped with rare earth elements such as Europium.

This is a provisional obviousness-type double patenting rejection.

Claims 5 and 6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14-16, 19-22, 24 and 31 of copending Application No. 12/293,486 (***copending appl. '486***) in view of Li et al (US 2004/0075083) as applied to claim 1 above, and further in view of Yates et al. (US 4,921,589).

Copending appl. '486 and Li have been discussed above.

However, they fail to teach covalently attaching 100 to 1000 molecules of organic fluorescent molecules to the coating of the nanoparticles and such organic fluorescent molecules are fluorescein or rhodamine.

Yates teaches applying a coating of polysiloxanes onto a substrate such as spheres or glass spheres (see col. 7, lines 10-22); Then applying a solution of photosensitizers such as fluorescein or rhodamine onto the polysiloxane coating. (see col. 4, line 50-col. 5, lines 13). Yates teaches the coating of polysiloxane of formula I, II or III on col. 5, line 43-col. 6, line 39) with m or n being integers of 200-2000 which represents how many molecules of siloxanes in the polysiloxane. Thus, when the photosensitizers are coated onto the polysiloxane, they would bind through the O-Si bond or C-Si bond of the polysiloxane (see col. 5, lines 13-16) and thus since there are

200-2000 siloxanes or O-Si or C-Si bonds are available, 200-2000 of organic fluorescent molecules would bind. The photosensitizer produces singlet oxygen which has a long enough lifetime to be chemically active in solution. The singlet oxygen is also a stronger oxidizing agent (see col. 1, lines 5-17).

Thus, one of ordinary skill in the art would have been covalently attach Rhodamine or Fluorescein onto polysiloxane coating of the nanoparticles in copending appl. '486 modified with Li by the method taught by Yates since these photosensitizers produce singlet oxygen which is a stronger oxidizing agent. One of ordinary skill in the art would have a reasonable expectation of success in combining these teachings since they all teach using polysiloxane coating on spheres.

This is a provisional obviousness-type double patenting rejection.

Claim 16 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14-16, 19-22, 24 and 31 of copending Application No. 12/293,486 (***copending appl. '486***) in view of Li et al (US 2004/0075083) as applied to claim 1 above, and further in view of O'Beirne (US 7,101,719 filed on Nov. 5, 2001).

Copending appl. '486 and Li have been discussed above.

However, they fail to teach 0.01% to 50 % of the metal cations of the nanosphere are uranide cations chosen from Ac, Th, Pa, Np, U, Pu.

O'Beirne teaches doping an inorganic host material such as yttrium oxide (see col. 6, lines 1-15) with an activator such as uranium. (see col. 6, lines 14-30).

Since it is well known in the art uranium can be used as an activator for doping inorganic host material such as yttrium oxide beside terbium, europium, erbium, etc., it would have been obvious to one of ordinary skill in the art to add uranium to yttrium oxide of copending appl. '486 modified with Li to obtain nanoparticles doped with rare earth metal cations such as uranium to produce a nanoparticle with a unique emission spectrum distinguished from the other nanoparticles doped with a different activator. One of ordinary skill in the art would have a reasonable expectation of success in combining these teachings since they all teach doping nanoparticles with rare earth metal cations.

This is a provisional obviousness-type double patenting rejection.

Claims 17 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14-16, 19-22, 24 and 31 of copending Application No. 12/293,486 (***copending appl. '486***) in view of Li et al (US 2004/0075083) as applied to claim 1 above, and further in view of Kresse et al. (US 5,427,767).

Copending appl. '486 and Li have been discussed above.

However, they fail to teach adding  $U^{235}$  or  $Gd^{157}$ .

Kresse teaches that: "Another possible approach to therapy can be taken by insertion of **157Gd** into ferrites and accomplishing neutron activation for thermal and epithermal neutrons taking advantage of the large capture cross section of **157Gd**. As in resonant nuclear absorption through photons (Mossbauer) described above, tissue



containing no  $^{157}\text{Gd}$  will scarcely take up neutrons and consequently will not be detrimentally affected. Neutron uptake is primarily concentrated on the areas containing  $^{157}\text{Gd}$ . Hence, sufficient enrichment of the tumor provided, radiation damage is inflicted only on the tumor by secondary radiation (Auger electrons and photons). The particles must be doped with the appropriate isotopes for application of ferrite/magnetite in therapy. (see col. 5, lines 34-45).

Since Kresse teaches doping magnetic nanoparticles with  $^{157}\text{Gd}$  for application in cancer therapy, it would have been obvious to ordinary skill in the art to incorporate  $\text{Gd}^{157}$  as an activator or dopant into the magnetic host of copending appl. '486 modified with Li to obtain nanoparticles doped with  $\text{Gd}^{157}$  for use in cancer therapy. One of ordinary skill in the art would have a reasonable expectation of success in combining these teachings because they all teach using Gd as a dopant in magnetic hosts, i.e.  $\text{Y}_2\text{O}_3$ .

This is a provisional obviousness-type double patenting rejection.

Claim 23 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12, 14-16, 19-22, 24 and 31 of copending Application No. 12/293,486 (***copending appl. '486***) in view of Li et al (US 2004/0075083) as applied to claim 1 above, and further in view of Molina et al. (Chem. Mater. 2001, 13, 2818-2823).

Copending appl. '486 and Li have been discussed above.

However, they fail to teach a water-soluble polymer such as dextran or polyethylene glycol is grafted onto the coating of the nanoparticle.

Molina teaches mixing polyethylene glycol with siloxane to coat  $\text{Eu}^{3+}$  and such coating offers high visible transparency, flexibility and good chemical stability. When these materials contain Europium ions, potentially interesting phosphor are obtained. The nature of the  $\text{Eu}^{3+}$  first coordination shell in these hybrids of polyethylene and siloxane may be tuned, as a function of both the salt concentration and the polymer molecular weight. (see entire document especially pg. 2818, col. 2).

Thus, it would have been obvious to one of ordinary skill in the art to combine polyethylene glycol and siloxane or polysiloxane as the coating to coat  $\text{Eu}^{3+}$  to obtain nanoparticles with a shell of high visible transparency, flexibility and good chemical stability (see Molina p. 2818, col.2 ) as taught by Molina. One of ordinary skills in the art would have a reasonable expectation of success in combining the teachings of Molina with copending appl. '486 modified with Li since they all teach using nanoparticles doped with Europium ions.

This is a provisional obviousness-type double patenting rejection.

### ***Response to Arguments***

Applicant's arguments, see Applicants' response, filed April 29, 2011, with respect to claims 1-24 have been fully considered and are persuasive. The rejections of 103 have been withdrawn.

Applicants argue mainly that one of ordinary skill in the art would not combine the teachings of Li and Bazzi because they do not teach the same matrix material.

Regarding the Obvious Type Double Patenting rejections, Applicants did not address these rejections in the response filed on April 29, 2011. Thus, these rejections are maintained.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PENSEE DO whose telephone number is (571)272-0819. The examiner can normally be reached on Monday-Friday, 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Application/Control Number: 10/591,465  
Art Unit: 1641

Page 11

/Mark L. Shibuya/  
Supervisory Patent Examiner, Art Unit 1641